REMARKS

Introductory Comments

Reconsideration of the above-identified application in view of the foregoing arguments is respectfully requested.

Claims 7, 10, 12-14 and 16 are pending and under consideration. Claims 8-9 have been canceled in this amendment. Claims 7, 10, 12-14 and 16 have been amended to delete the "fragment" language as noted below. No new matter has been added as a result of these amendments.

Objection to the Title

The Examiner states that the title is not descriptive of the elected invention. Applicants have amended the title. If the Examiner finds the new title objectionable, Applicants respectfully request the Examiner's suggestion in amending the title.

Objection of Claims 8-9 Under 37 C.F.R 1.75(c)

Claims 8-9 are objected to under 37 C.F.R 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Specifically, the Examiner states that these claims are drawn to a particular means by which a polypeptide is produced, i.e., by recombinant or synthetic techniques, but these limitations do not appear to structurally change the polypeptide as claimed in claim 7.

Applicants have canceled claims 8-9 and the objection is now moot.

Rejection of Claims 7-10, 12-14 and 16 Under 35 U.S.C. § 101

Claims 7-10, 12-14 and 16 are rejected under 35 U.S.C. § 101 for not being supported by either specific or substantial asserted utility or a well established utility. Specifically, the Examiner states that while the specification

discloses that a consensus sequence pertaining to the invention was found to be more than 82 times more often in the GI tract tissues than non GI tract tissues, there is no indication as to the presence or frequency of normal expression versus cancerous expression or diseased expression. The Examiner further states that the specification does not discuss studies or assays using the claimed SEQ ID NOS: 41-49.

The Examiner asserts that polypeptides have very significant divergent functions. The Examiner alleges that WO 01/68848 discloses an amino acid sequence, namely SEQ ID NO: 129 which is 99.6% identical to SEQ ID NO: 41, but is used to detect colon, lung or prostate tumors. The Examiner also alleges that WO 99/963088 (herein "WO '088") discloses a polypeptide sequence that is 99.7% identical to SEQ ID NO: 41 which has functions pertaining to channel proteins and adhesion molecules. The Examiner cites several other disclosures of proteins with sequences having high percent identity in comparison with the instant sequences while having different functions as compared to what is disclosed by Applicants. Thus, the Examiner posits that based on these prior art, Applicants' assertion regarding the utility of the claimed sequence is questionable for detection of GI tract diseases.

Applicants respectfully traverse this line of reasoning from the Examiner's rejection. A variety of wheels that have similar designs can still be considered novel and non-obvious although the wheels have different or better utilities. For example, a wheel that is similar in the overall design but is thinner than another can be better suited in a bicycle versus a scooter. The Examiner has cited several post-filing date references in order to convey her point regarding divergent functions of the polypeptides. These references are not prior art as they are filed or published after Applicants' filing date. However, Applicants would like to address this argument pertaining to these references now.

The Examiner has not provided a specific sequence beside SEQ ID NO: 129 of WO '088 from these post-fling art nor an alignment for such in comparison to the sequences in the instant claims.

Applicants note that these post-fling art cited above are large documents. Most of the cited documents contain a large number of sequences. Applicants respectfully request that the Examiner clearly state which sequences the Examiner is referring to and to provide a sequence alignment. Applicants note the following with respect to SEQ ID NO: 129 of WO '088 which the Examiner alleges has a 99.6% identity with Applicant's SEQ ID NO: 41. Applicants SEQ ID NO: 41 contains 917 amino acids and therefore 2,751 nucleotides. SEQ ID NO: 129 of WO '088 contains only 1,528 nucleotides. The Examiner has not provided a sequence alignment showing any matching of nucleotides for these two sequences. Nevertheless, even if there is a high percent of nucleotide matches, the percent identity between these two sequences cannot be 99.6% as alleged by the Examiner since SEQ ID NO: 41 contains 2,751 nucleotides while SEQ ID NO: 129 only contains 1,528 nucleotides.

The Examiner states that there is no disclosure in the specification as to exactly what diseases are diagnosed using the instant sequences and therefore there is no disclosure of a specific utility (page 5 of the Office Action). Applicants respectfully traverse this line of argument. As noted by the Examiner, page 1, lines 12-15 of the specification states that the instant sequences may be used to detect cancer of the GI tract. Applicants submit that one of ordinary skill in the art would be able to differentiate GI cancer from a normal healthy state of an individual, or other types of cancer and this would be considered a specific disease. The specification provides examples of organs of the GI tract that are considered within the realm of GI tract cancer, such as the esophagus, stomach, small and large intestines, rectum and pancreas (page 1, lines 16-17). As noted on page 2, lines 5-17, other procedures used to further confirm cancer include barium studies, endoscopy, biopsy and computed tomography. No single detection procedure is one hundred percent accurate at very early stages of cancer development. However, this does not take away its utility as more than one procedure may be used in concert in detecting and verifying cancer development. The Examiner's standard of pinpointing the exact location or organ of cancer and extremely high accuracy of cancer detection is not practical. If this

were the case, then according to the Examiner, many of the beneficial procedures already known with respect to cancer detection serve no value or utility.

On page 51, line 10 to page 52, line 9, Applicants disclose that expressed sequence tags (ESTs) relevant to the present invention were used in diagnosis. ESTs corresponding to the consensus sequence of CS193 (SEQ ID NO: 18) were found in 18.6% of GI tract tissue libraries. However, ESTs corresponding to the consensus sequence of CS193 were found in only 0.35% of other non-GI tract tissue libraries. Therefore, the consensus sequence was found in more than 82 times more often in GI-tract than non-GI tract tissues. Just as PSA and CEA which are used to detect prostate cancer and colorectal cancer by detecting these proteins in the circulation of patients, detection of the instant polypeptides at distant sites can be used as an indicator of diseases of the tract (page 3, lines 18-32).

The Examiner also alleges that there is no substantial utility for the claimed polypeptides since it is disclosed that the claimed polypeptide can be used to obtain an antibody (pages 5-6 of the Office Action). Applicants submit that the utility of antibodies against the claimed polypeptide proves the opposite of the Examiner's contention, that the claimed polypeptides indeed have a substantial utility. On page 7, lines 26-35 of the specification, it is disclosed that an antibody that binds to at least one epitope of the CS193 antigen can be used to diagnose the diseases at issue by contacting with a test sample, in order to form antibody/antigen complexes. The detection of the presence of these complexes is an indication of the presence of CS193 antigen. The utility of antibody/antigen complexes in evaluating diseases is well known in the art. See for example, *Immunobiology*, 5th Ed., Janeway et al., Garland Publishing (2001), pages 566-571. Antibody/antigens of the following have been shown as an indication of the following tumor type: cyclin-dependent kinase 4 for melanomas, beta-catenin for melanoma, caspase-8 for squamous cell carcinoma, MAGE-1 and MAGE-3 for melanoma breast glioma, HER-2/neu for breast and ovary tumors, and MUC-1 for breast and pancreas tumors for example.

The Examiner categorizes the instant polypeptides as a starting material that is used to produce a final product. Applicants fully traverse the Examiner's categorization of the instant polypeptides as a mere starting material. As stated above, the instant sequences were derived from consensus sequences and these peptides are useful for several methods of disease detection. The peptides therefore can at least be categorized as intermediate products which have useful and substantial utility. Such intermediate products, especially their uses, have been differentiated from starting materials and have been determined by the courts to have practical utilities.

For the reasons set forth above, Applicants respectfully request withdrawal of the rejection of claims 7-10, 12-14 and 16 under 35 U.S.C. § 101 for not being supported by either specific or substantial asserted utility or a well established utility.

Rejection of Claims 7-10, 12-14 and 16 Under 35 U.S.C. § 112, First Paragraph-Enablement

Claims 7-10, 12-14 and 16 are rejected under 35 U.S.C. § 112, first paragraph, as failing to provide an enabling disclosure. The Examiner states that since the claimed invention is not supported by either a specific or substantial asserted utility or a well-established utility for the reasons set forth above, one skilled in the art would not know how to use the claimed invention. Applicants respectfully traverse the rejection.

The Examiner reiterates arguments stated above. Accordingly, Applicants arguments above are incorporated herein.

Rejection of Claims 7-10, 12-14 and 16 Under 35 U.S.C. § 112, First Paragraph-Written Description

Claims 7-10, 12-14 and 16 are rejected under 35 U.S.C. § 112, first paragraph as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant

art that the inventors, at the time the application was filed, had possession of the claimed invention. Applicants respectfully traverse the rejection.

The Examiner reiterates the rejection made above. Applicants hereby incorporate the arguments presented above.

The Examiner further states that Applicants' Example 13 is directed to protein variants and the specification does not indicate what distinguishing attributes are shared by the members of the genus. According to the Examiner, the limits placed upon the number of amino acid substitutions, deletions, insertions and/or addition that may be made to SEQ ID NO: 41-49 is limitless on the ends of the proteins. Therefore, it appears that the Examiner is implying that since there is no limit on the length of the fragments, the actual polypeptide may have more than 15% change as allowed by the claim language. Applicants fully traverse the Examiner's contention regarding the limit of change based on amino acid substitutions, deletions, insertions and additions and that based on the fragment language that the actual polypeptide may have more than a 15% change.

Applicants would like to first address the Examiner's argument that based on the fragment language, the actual polypeptide may have more than a 15% change. Applicants have amended the claims to require the fragment to have a length of at least 15 amino acids. The claims recite the phrase "fragments thereof" which requires these fragments to be a subunit of the claimed polypeptide sequence, namely SEQ ID NOS: 41-49. Additionally, Applicants' claims use a Markush grouping which consists of SEQ ID NOS: 41-49 and fragments thereof having a length of at least 15 amino acids. Therefore, the fragments cannot be interpreted to be "open-ended" and have more than 15% change or less than 85% identity, as interpreted by the Examiner.

The inquiry into whether the description requirement is met is determined on a case-by-case basis and is a question of fact. Section 2163 *Manual of Patent Examining Procedure* (8th Edition, Rev. 1, Feb. 2003). When a question regarding the adequacy of the written description arises, the fundamental factual inquiry is whether the specification conveys to those skilled in the art, as of the

filing date sought, that applicant was in possession of the invention being claimed. Section 2163.02 *Manual of Patent Examining Procedure* (8th Edition, Rev. 1, Feb. 2003). Possession can be shown in a number of ways. For example, an Applicant can show possession by: (1) an actual reduction to practice of the claimed invention; (2) a clear depiction of the invention in detailed drawings or in structural chemical formulas which permit a person skilled in the art to clearly recognize that applicant had possession of the claimed invention; or (3) any description of sufficient, relevant, identifying characteristics so long as a person skilled in the art would recognize that the inventor had possession of the claimed invention. *Id.*

A description as filed is presumed to be adequate, unless or until sufficient evidence or reasoning to the contrary has been presented by the Examiner to rebut the presumption. Section 2163.04 *Manual of Patent Examining Procedure* (8th Edition, Rev. 1, Feb. 2003). The Examiner, therefore, must have a reasonable basis to challenge the adequacy of the written description. *Id.* The Examiner has the initial burden of presenting by a preponderance of the evidence why a person skilled in the art would not recognize in an applicant's disclosure a description of the invention as defined by the claims. *Id.* "A general allegation of unpredictability in the art is not a sufficient reason to support a rejection for lack of adequate written description." *Id.* The *Manual of Patent Examining Procedure* even cautions Examiners that "rejection of an original claim for lack of written description should be rare." (See Section 2163 *Manual of Patent Examining Procedure* (8th Edition, Rev. 1, Feb. 2003)).

The U.S. PTO has issued Guidelines governing its internal practice for assessing whether the specification contains an adequate written description of the invention being claimed. In its Guidelines, the PTO has determined that the written description requirement can be met by "show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics..., i.e., the complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of

such characteristics. Utility Examination Guidelines, Federal Register, Vol. 66, No. 4, pages 1092-1099, January, 2001 *Guidelines*, 66 Fed. Reg. at 1106.

Contrary to the arguments made by the Examiner, Applicants submit that the specification adequately describes the polypeptides encompassed within the scope of the invention being claimed. First, as specifically recommended by the *Guidelines*, Applicants have provided the complete structure of the claimed polypeptides as demonstrated in SEQ ID NOS: 41-49. Second, with respect to the issue raised by the Examiner regarding the "numerous structural variants" and the "number of amino acid substitutions, deletions and/or additions that may be made to the claimed polypeptides", Applicants submit that because the level of skill in the area of molecular biology is considerably high, one of ordinary skill in the art, after reviewing Applicants specification, would clearly recognize that the Applicants have provide an adequate written description of the variants, substitutions, deletions and/or additions encompassed by the claims. Applicants specifically direct the Examiner's attention to page 23, lines 29-36 of the specification where it states that "Thus a polypeptide of the present invention may have an amino acid sequence that is identical to that of the naturally occurring polypeptide or that is different by minor variations due to one or more amino acid substitutions. The variation may be a 'conservative change' typically in the range of about 1 to 5 amino acids, wherein the substituted amino acid has similar structural or chemical properties, e.g., replacement of leucine with isoleucine or threonine with serine. In contrast, variations may include nonconservative changes, e.g., replacement of a glycine with a tryptophan. Similar minor variations may also include amino acid deletions or insertions, or both. Guidance in determining which and how many amino acid residues may be substituted, inserted or deleted without changing biological or immunological activity may be found using computer programs well known in the art, for example, DNASTAR software (DNASTAR Inc., Madison, WI)." As illustrated by the above cited portion of the specification, computer programs are available to those of ordinary skill in the art and these programs can be used in providing guidance in determining "which and how" many amino acids residues in SEQ ID

NOS: 41-49 can be substituted, inserted or deleted. The use of such programs is well known to those of ordinary skill in the art.

Therefore, in view of the aforementioned arguments, Applicants submit that one of ordinary skill in the art would clearly recognize that Applicants had possession of the claimed invention and have provided an adequate written description. Thereupon, Applicants respectfully submit that the Examiner has failed to provide sufficient factual evidence to rebut the presumption that the description as filed is inadequate. Moreover, the Examiner fails to present any factual evidence as to why a person of ordinary skilled in the art would not recognize in Applicants disclosure a description of the invention as defined by the claims. In view of the absence of such evidence, Applicants submit that this rejection should be withdrawn.

Rejection of Claims 7-10, 12-14 and 16 Under 35 U.S.C. § 102(b)

Claims 7-9, 12-14 and 16 are rejected under 35 U.S.C. § 102(b), as being anticipated by Cunningham *et al.*, *J. Biol. Chem.* (1995) 270(52):31016-31026 (herein "Cunningham"). Applicants respectfully traverse the rejection.

The Examiner states that Cunningham discloses a polypeptide that is 100% identical to SEQ ID NO: 41. The polypeptide the Examiner refers to only has 8 amino acids. Applicants are perplexed as to how this peptide is therefore considered to have 100% identity as compared to SEQ ID NO: 41 which has 917 amino acids. Applicants have amended the claims to require the fragments to have a length of at least 15 amino acids. Support for this amendment can be found on page 14, lines 33-36.

Accordingly, Applicants respectfully request the withdrawal of the rejection of claims 7-10, 12-14 and 16 under 35 U.S.C. § 102(b), as being anticipated by Cunningham *et al.*

CONCLUSION

Applicants respectfully submit that the claims comply with the requirements of 35 U.S.C. Sections 101, 112, and 102. Accordingly, a Notice of Allowance is believed in order and is respectfully requested.

Should the Examiner have any questions concerning the above, she is respectfully requested to contact the undersigned at the telephone number listed below. If the Examiner notes any further matters which the Examiner believes may be expedited by a telephone interview, the Examiner is requested to contact the undersigned.

If any additional fees are incurred as a result of the filing of this paper, authorization is given to charge deposit account no. 23-0785.

Respectfully submitted,
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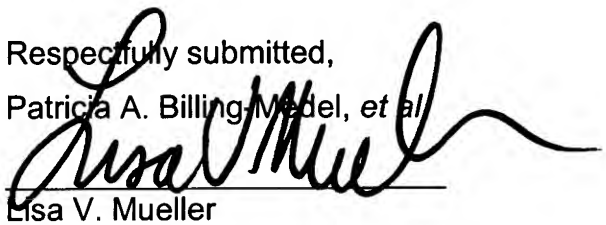

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